Transient Ventricular Conduction Disturbances Produced by Intra-atrial Injection of Single Doses of KCl

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ABSTRACT

In dogs under pentobarbital anesthesia, the administration of KCl in single intra-atrial doses of 1 mg/kg produced varying effects on intraventricular conduction depending upon the initial potassium concentration of systemic blood. At normal and moderately increased systemic K concentrations, single injections of KCl improved intraventricular conduction, but at higher systemic K concentrations a negative dromotropic effect appeared. Following injection into the right atrium, the effect appeared immediately in the right ventricle, followed after some delay by an appreciably lesser effect in the left ventricle. Injection of potassium into the left atrium altered conduction in the left ventricle without affecting the right ventricle. The results indicate that transient alterations of [K] in the blood of the ventricular cavity can act directly on the specialized conduction network to alter the rate of intraventricular conduction.

ADDITIONAL KEY WORDS

Purkinje system plasma [K+] bundle branch block anesthetized dogs

Methods

The experiments were performed on mongrel dogs weighing 10 to 15 kg and anesthetized by intravenous injection of sodium pentobarbital in a dose of 35 mg/kg. Under artificial respiration, the thorax was opened in the midline, and the heart was exposed and suspended in the opened pericardium. The heart was decentralized acutely by cutting both cervical vagi.
and excising the stellate and upper thoracic sympathetic ganglia on both sides.

The bipolar stimulating and recording electrodes were small steel hooks. A pair of stimulating electrodes was attached to each ventricle at the anterior epicardial surface close to the base of the ventricles. A pair of recording electrodes was also attached to each ventricle at a distance of about 50 mm from the stimulating electrodes. Tektronix waveform and pulse generators were used to deliver basic stimuli to the stimulating electrodes through an isolation transformer. These stimuli were rectangular pulses of 2-msec duration at twice the diastolic threshold.

Intraventricular conduction time was determined by measuring the interval between the stimulus artifact and the response at the remote recording electrodes on the same ventricle. The recorded value includes, of course, any latency at the stimulated site. However, no measurable change in threshold at the epicardial surface occurred during the time course of the effects of acute single injections of KCl. The stimulus-response interval was measured from photographs of superimposed oscilloscope traces at a high sweep speed or from traces recorded on a Grass polygraph. An Electronics for Medicine recorder was used in some experiments for simultaneous recording of the epicardial electrograms and right and left intraventricular pressures. The pressures were recorded by means of Statham pressure transducers attached to cannulas introduced into the ventricular cavity through the free wall.

The postassium concentration of systemic blood was increased by infusion of a solution of KCl through a femoral vein at a rate of 1.5 to 2 mg/kg per min. Samples of the arterial blood were drawn from a femoral artery at various intervals during the KCl infusion for determination of plasma [K] by means of flame photometry. For a sudden and brief increase of [K] in the intraventricular blood, KCl (20 mg/ml) was injected rapidly in a dose of 1 mg/kg through a cannula inserted into the atrium on the same side.

In a few experiments the effects of increased external [K] were studied in isolated preparations of dog false tendon and papillary muscle in vitro. Transmembrane action potentials of Purkinje and muscle fibers were recorded simultaneously during exposure to Tyrode's solution containing 2.7 and 8.1 mM KCl. The action potentials were differentiated to permit estimation of the maximum rate of rise (dV/dt) of the upstroke of the action potential in each state.

Results

Because of the biphasic effect of increasing [K] on intraventricular conduction, a given amount of potassium should either decrease or increase the conduction time depending upon the initial K level of systemic blood. To demonstrate both phases, single intraatrial doses of KCl (1 mg/kg) were superimposed upon a continuous infusion of KCl at a rate chosen to cause a slow progressive increase of plasma [K]. Figure 1 shows the effects of transient increases of [K] in the blood in the right ventricular cavity upon right ventricular conduction during the course of such an infusion. In each segment of the figure, successive sweeps were superimposed with the camera shutter open until the maximum effect of the single intra-atrial injection was reached. The arrow in each case indicates the conduction time just prior to injection. Segment A was recorded just before the infusion was begun, at a plasma [K] of 3.6 mEq/liter; B, C, D, and E were recorded as the systemic plasma [K] was progressively increased to 5.4, 6.6, 7.8, and 8.6 mEq/liter, respectively. The preinjection conduction times (arrows) reflected the basal K concentrations: 59 msec in A, decreasing to 55 and 53 msec in B and C, and increasing to 61 and 67 in D and E. The rapid injection

![Figure 1](http://circres.ahajournals.org/)

Effects of injection of single doses of KCl into the right atrium upon right ventricular conduction time. Basal [K] of systemic arterial blood: A, 3.6 mEq/liter; B, 5.4 mEq/liter; C, 6.6 mEq/liter; D, 7.8 mEq/liter; and E, 8.6 mEq/liter. The sweeps were triggered by the ventricular driving stimuli; electrograms were recorded at about 50 mm from the site of stimulation.
of single additional doses of KCl caused a slight reduction of conduction time in A and B, and progressively increasing prolongation in C, D, and E. In E the increment was 21% of the preinjection value.

The observed effects of potassium injected into the right atrium appeared within 5 sec, reached a peak in little more than 10 sec, and were nearly dissipated at about 30 sec. The speed of development and the brief duration suggest that the effects were not the result of an increase in [K] in the coronary blood, but must have been due to the transient elevation of [K] within the right ventricular cavity.

Further evidence that the effect of the injected KCl was exerted directly on the subendocardial specialized conducting system and not by way of intramural perfusion is illustrated in Figure 2. In this experiment, recording electrodes were attached to the epicardial surface of the left ventricle at sites close to, and at a distance of about 5 cm from the stimulating electrodes (Va and Vb, respectively). Before the intravenous infusion of KCl was begun, the plasma [K] was 4.7 mEq/liter, and the conduction times measured from the stimulus artifact to the peak of the recorded responses at Va and Vb were 18 msec and 64 msec, respectively. Injection of KCl into the left atrium caused no significant change in either value. When systemic plasma [K] had been increased to 8.6 mEq/liter, the basic conduction times were increased to 20.5 and 72 msec at the near and distant points. Intra-atrial injection of KCl now caused a progressive increase to a maximum of 80 msec in the interval recorded at Vb, but did not significantly alter the conduction time to the nearer point, Va (Fig. 2). The results suggest that conduction was not disturbed within the radius of presumably intramural propagation (7), but it was impaired in the subendocardial Purkinje network.

Single dose injections of KCl into the right atrium, although large enough to cause an abrupt elevation of perhaps 1 to 2 mEq/liter in the right intraventricular cavity, were not large enough to cause a measurable increase in systemic arterial plasma [K] after one circulation. Accordingly, the right ventricular conduction time returned promptly to preinjection levels (Fig. 3). After a single passage through the pulmonary circulation, however, the potassium concentration was still high enough to cause significant depression of conduction in the left ventricle. In the experiment illustrated in Figure 3, injection of KCl into the right atrium caused a prompt increase of 27% in right intraventricular conduction time, followed, after a further latency of about 20 sec, by a lesser but significant prolongation of conduction in the left ventricle. On the other hand, in another experiment injection of the same dose into the left...
atrium caused a major change in conduction in the left ventricle without any significant change in the right (Fig. 4).

The results shown in Figures 3 and 4 suggest that the sequential local effects of K upon the subendocardial conducting system of the right and left ventricles should mimic first right, then left bundle branch block. This was demonstrable in the experiment illustrated in Figure 5. The heart was allowed to beat spontaneously with S-A (sino-atrial) nodal rhythm at a starting plasma [K] of 7.6 mEq/liter. The top trace in each part of the figure was recorded from electrodes attached to the right atrium (RA); the next two traces are the records from right and left ventricles (RV and LV), and the bottom trace is a record obtained from one each of the pairs of right and left ventricular electrodes (R-LV).

In the control panel A, activity at the right ventricular site preceded that at the left by 20 msec, and the combined R-LV recording was arranged to show an upright polarity. Panels B and C were recorded at the indicated intervals after the injection of KCl into the right atrium. In B, as the negative dromotropic effect reached its peak in the right ventricle, RV followed LV by 15 msec; the reversed order of activation was manifested by the inverted polarity of the R-LV complex. Panel C was recorded when the peak effect appeared in the left ventricle. Conduction was now delayed in the left ventricle and the RV-LV interval increased to 35 msec. Following the injection of KCl, the atrial electrograms disappeared almost completely (Fig. 5, B and C), although one-to-one sino-ventricular conduction persisted as in the experiments reported by Vassalle and Hoffman (8).

Delay in the activation of first the right, then the left, ventricle should also result in

![Figure 4](image_url)

**FIGURE 4**
The time course of effects of KCl injected into the left atrium on intraventricular conduction time of both ventricles. Systemic K concentration, 8.1 mEq/liter.

![Figure 5](image_url)

**FIGURE 5**
Serial effects of KCl injected into the right atrium upon the pattern of ventricular excitation. The traces were taken before the injection of KCl in A and at indicated intervals after the injection. Systemic K concentration, 7.6 mEq/liter.

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FIGURE 6
Influence of elevated [K] on transmembrane potentials of papillary muscle fiber (M) and Purkinje fiber (P) of isolated preparation of dog right ventricle. Zero potential line indicated in each trace. Differentiated action potentials recorded below on different time base. A, external [K] = 2.7 mM; B, 8.1 mM.

Corresponding alterations in the sequence of contraction of the two chambers. This was demonstrated in an experiment in which, in addition to the electrical records, pressure curves were recorded from both ventricles. Systemic plasma [K] was increased to 7.8 mEq/liter by continuous infusion of KCl. Gross impairment of intra-atrial conduction at this concentration was apparent in the RA electrogram. The onset of left ventricular contraction, as determined from the records of intraventricular pressures, preceded that of the right by 12 msec. Eight seconds after the injection of KCl into the right atrium, conduction was delayed in the right ventricle, and the R-LV complex was reversed, as in the experiment of Figure 5. The onset of contraction was delayed by 12 msec in the right ventricle. As a result, the beginning of isometric contraction in the left ventricle preceded that in the right by 24 msec. After recovery from the right atrial injection of KCl, a second dose was injected into the left atrium. After 8 sec, conduction was delayed in the left ventricle, as indicated by a broader R-LV complex. The onset of contraction was now simultaneous in both ventricles.

Reduction of the resting membrane potential and of the velocity of depolarization are well known effects of high [K] in ventricular muscle and in the specialized conducting tissue, but we could find no published studies in which simultaneous observations of the two tissues were recorded. Because the effects of brief exposure to elevated [K] appeared to be exerted predominantly on the subendocardial Purkinje network, in vitro studies of the comparative effects of increased [K] on muscle and Purkinje tissue were made. The results of such an experiment are illustrated in Figure 6. Transmembrane potentials and the differentiated action potentials were recorded from papillary muscle and false tendon in a preparation excised from the right ventricle of a dog. The preparation was driven at a constant frequency by stimuli applied through bipolar extracellular electrodes to the papillary muscle. In panel A, the records were taken at [K] = 2.7 mM; in panel B records from the same cells are shown after 10 min of exposure to [K] = 8.1 mM. The resting membrane potential of each fiber was decreased, by 9% in the muscle and 22% in the Purkinje fiber; the maximum rate of rise was also decreased, by 39% in muscle and 60% in Purkinje.

Discussion
The results described above indicate that the rate of intraventricular conduction can be altered by a brief increase in the potassium concentration of blood in the ventricular cavity. The effects developed within 5 to 10 sec after the introduction of KCl into the ventricle, and were substantially over in less than a minute. The conduction time was either decreased or increased, depending on the initial potassium concentration of the systemic blood; it was slightly decreased when the systemic K level was normal or moderately elevated, and markedly increased when the systemic K level was further elevated. At plasma levels above 7.0 mEq/liter, further increments in [K] caused relatively great increments in conduction time; accordingly, the changes resulting from single small doses were greater at higher initial potassium levels. The marked negative dromotropic effect of additional potassium during hyperkalemia is presumably due to further reduction of the resting membrane potential to a level at
which the Na permeability mechanism is greatly impaired.

Although the effects of increased [K] are qualitatively similar in atrial and ventricular myocardial cells and in the Purkinje fibers of the ventricle (3), the effects observed appear to be almost completely the result of an action on the subendocardial Purkinje network. The in vitro experiments suggest that the Purkinje fibers appear to be more sensitive than muscle to elevated [K], but the effects of single injections on conduction time in vivo are more probably the result of the anatomical relationships. In the experiment of Figure 4, for example, left atrial injection of KC1 caused no significant alteration of conduction time in the right ventricle, but the concentration of [K] in the coronary arterial blood must have reached the same level as that in the left ventricle. The additional delay and dilution imposed by diffusion from coronary capillaries into the extracellular fluid may, of course, have reduced the increment in concentration, but it also seems likely that a substantial fraction of the nutritive supply of the subendocardial fibers must be derived from the blood in the ventricular cavity. When [K] is gradually elevated, all of the tissue would then be exposed to the same extracellular concentration, but a brief additional slug would influence primarily the Purkinje system. This is apparent in Figure 2. Slow elevation of plasma [K] from the initial level of 4.7 to 8.6 mEq/liter caused approximately the same percentage increase of conduction time at the near and distant recording sites, but the additional slug caused a significant further depression only at the distant point.

The rapid and direct action of K on the Purkinje network makes it possible to produce intraventricular conduction disturbances in either ventricle at will. The procedure can serve as a useful model of bundle branch block in studies of impulse propagation and correlated mechanical events.

References

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